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INSECT TUMORS

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Willis (1948) defined a tumor as, ". . . an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of normal tissue, and persists in the same excessive manner after cessation of the stimuli which evoked the change." These abnormal masses can be further characterized as follows:

1. They are cellular in nature, appear at specific sites and may spread or metastasize.
2. Their incidence is affected by X-irradiation and nutritional variation.
3. They can be transplanted from one to another of the same species.
4. Hereditary factors for susceptibility are present.

By far the greater amount of investigation has been carried on with tumors of mammals while those of insects have received less attention. In general, insect tumors are similar to those of mammals except that they may regress during metamorphosis and they are sensitive to temperature changes.

The basic tumor process can be divided into two major phases; genesis and growth. During genesis the normal intra-cellular processes are upset in some way (tumor-inducing action), possibly through the loss of a strategic enzyme or by the alteration of specific substrates, and the tumor process is initiated. The end of the generative process may be identified by structural modifications of the "changed" cell. The onset of division in the tumor cell introduces the growth phase and terminates in an abnormal mass of cells which may spread to the other regions of the organism.

Except for the hereditary tumors of *Drosophila*, most of the reported insect tumors have not been analyzed with respect to their cellular constituents, or to their possible effects on the normal physiological activities of the insect. Naturally occurring tumors have been observed in six orders and induced (provoked by man) tumors have been noted in two. The available data are summarized in Table 1.

Table 1. Summary of tumors reported in insects

Type of tumor	Order	Genus	Reference
1. Spontaneous	Hymenoptera	Apis	White (1921)
		Bombus	Palm (1949)
		Formica	Brun (1925)
	Coleoptera	Phytodecta	Balazuc (1948)
	Orthoptera	Gryllotalpa	Palm (1948)
2. Parasitic	Ephemerida	Hepatagenia	Codreanu (1935)
		Ritherogenia	
	Hymenoptera	Gilpinia	Bird (1949)
3. Induced			
a. surgically	Orthoptera	Dixippus	Pflugfelder (1938)
		Leucophaea	Scharrer (1944; 1948)
b. nutritionally	Diptera	Drosophila	Hartung (1955)
4. Hereditary	Diptera	Drosophila mel. (25 strains)	Stark (1918; 1937) Burdette (1951)
	Lepidoptera	Pygaera	Federly (1936)

The pigmented tumors in *Drosophila*, the insect which has been used so extensively in the development of Genetics, have been vigorously investigated ever since these abnormal growths were first described by Stark (1918). There are several reasons which invite intensive study of these strains:

1. The chromosome number is small (8), and the gene loci of each chromosome has been adequately mapped thereby permitting the isolation of many pure strains; a condition not often realized in vertebrate studies.

2. Their life cycle is short—approximately 10 days from egg to

adult.

3. Environmental conditions (food, temperature, humidity) can be easily controlled thus permitting large colonies.

One of the most interesting types of tumors to be found in *Drosophila melanogaster* is a pigmented one called a melanoma which appears during the larval period. The gene thought to be responsible for tumor induction is usually found on the second chromosome. Other genes acting as modifiers also may be present. Manipulation of the nutritional environment of these tumor strains, such as by the feeding of the amino acid tryptophan (Plaine and Glass 1955) and by increasing the concentration of specific "B" vitamins in the media (Friedman 1955), have been shown to increase the incidence of melanomas in this species. Tumor incidence can also be altered by interfering with the hormone balance (Burdette 1954). Also of interest is the observation by Burton (1955) that tumors can be induced in a non-tumorous strain by the injection of cell-free extracts of whole larvae of a tumorous strain.

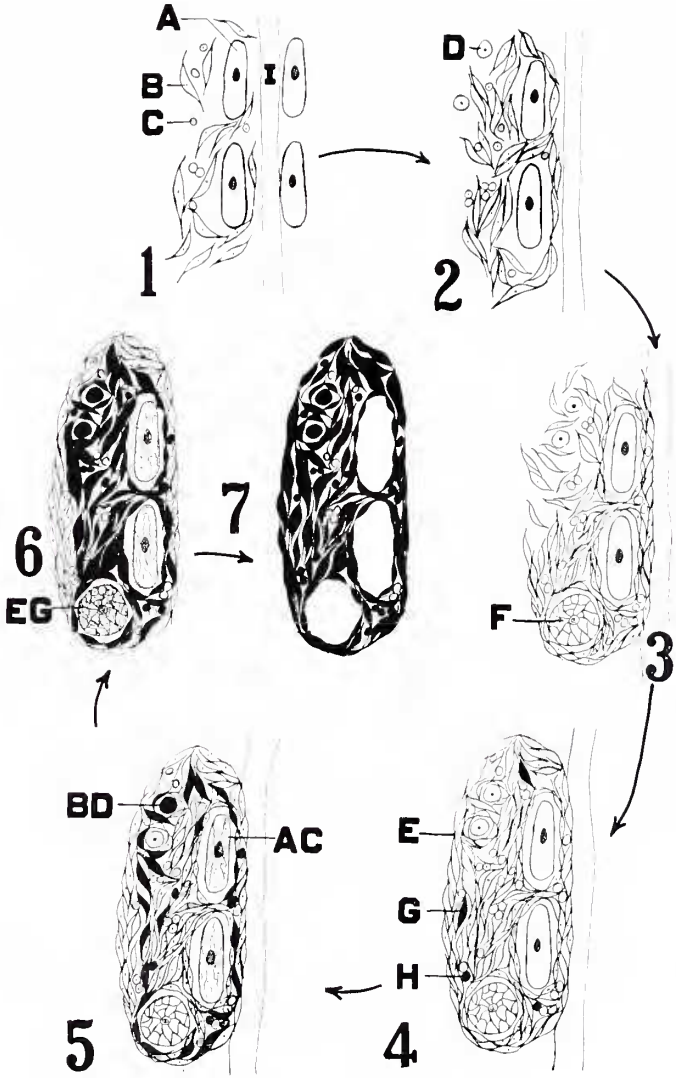
The development of vertebrate tumors has been extensively studied but, because of technical difficultis, little has been done with the development of insect tumors. Some of the difficulties have been overcome (Kaplan 1955) with particular reference to the histogenesis of the melanoma found in the *tu-e* strain of *Drosophila melanogaster* which is summarized here. At least six specific sites of tumor formation in the larva have been identified and their developmental histories elucidated. The chief site is the abdominal pericardial cell area, followed by the hemolymph, fat body, tracheal tubes, muscle, and imaginal discs. The common factor in the *tu-e* (tumorous) strain were spindle-shaped circulatory cells which first appeared in the caudal hemocoele at 72 hours of larval development.

Since the abdominal pericardial area tumor showed the greatest frequency, its development is described. (See plate). Three progressive phases can be identified in the development of the *tu-e* tumor. These are the, a) organization phase, b) enlargement phase, and c) melanization phase, which is divided into a peripheromelanotic stage and a centromelanotic stage. Since the process is a continuous one, some overlapping occurs in the figures used.

a During the organization phase, loose clusters of spindle cells (B) begin to aggregate around the abdominal pericardial cells (A), (Figs. 1 & 2); this aggregation is coupled with a rather slow increase in tumor size (Fig. 2) and occurs between 72 and 114 hours of larval development. Two types of spherical cells (C & D) become enmeshed in the organizing mass.

b) During the enlargement phase a major increase in tumor size

BULL. B. E. S. VOL. LI PLATE I



Figs. 1 & 2. Organization phase, (72–114 hours). Spindle cells (B) aggregating and isolating abdominal pericardial cells (A) located along the heart (I). Spherical cells (C & D) becoming enmeshed. Fig. 3. Enlargement phase, (114–120 hours). Major increase in tumor mass coupled with infiltration of the fat body

occurs (Fig. 3) in which individual pericardial cells are surrounded by large numbers of spindle cells. At this time adjacent fat cells (F) are incorporated in the tumor mass. In one such tumor, approximately 660μ in length, seven morphologically intact fat cells as well as six intact pericardial cells were counted. The end of the enlargement phase is indicated by the completion of a spindle cell sheath (E) which encloses the tumor mass (Fig. 4).

c) During the melanization phase (Figs. 4, 5, 6, 7) there is a gradual breakdown of some cellular components and a deposition of pigment (melanization) in others.

i) The breakdown of normal pericardial cells (AC) is first indicated in figure 5 and of the fat cells (EG) in figure 6. The destruction of these cells within the tumor mass and their maintenance in normal form in other body areas is clearly unusual.

ii) The onset of melanization is first indicated in figure 4 and occurs only in the spindle cells (G) and spherical cells (H & BD). Melanization in the *tu-e* tumor is an intra-cellular process, occurring only in those cells which are part of the tumor mass. The process of melanin deposition begins in the peripheral cells and progresses from cell to cell until all that remains of the tumor is an acellular mass containing necrotized fat and pericardial cells (Figs. 5, 6, 7).

Discussion

The *tu-e* tumors of Drosophila arise from abnormal spindle cells circulating in the hemolymph of the larvae which aggregate about certain normal cells (chiefly pericardial but also fat) at specific sites. The pigmented tumors are not destroyed (histolyzed) during pupal metamorphosis and persist in the adult as acellular melanotic masses. The exact origin of the responsible spindle cells is not known, but the association of spindle cells and tumorous strains in general is well established; conversely the absence of spindle cells

(F) by spindle cells. Fig. 4. Melanization phase, (114–120 hours). Onset of melanin formation in spindle (G) and spherical cells (H). Completion of the spindle cell sheath (E). Fig. 5. Peripheromelanotic stage, (120–126 hours). Melanized tumor cells are now arranged in a ring surrounding the central amelanotic mass. Pericardial cells are becoming necrotic (AC). Large spherical cells are melanized (BD). Fig. 6. Centromelanotic stage, (pupa and/or adult). The tumor mass has become completely melanized except for the peripheral sheath. Fat cells are now necrotic (EG). Fig. 7. Completely melanized, acellular mass, (pupa and/or adult).

in non-tumorous strains is recognized. It has also been demonstrated that spindle cells which have not undergone histological change (melanization) are destroyed during pupal metamorphosis while those that have melanized to any degree persist into the adult (Moser 1956).

Melanin deposition is a normal biological process found in a wide variety of animal tissues, both invertebrate and vertebrate, which basically involves the enzymatic polymerization of the amino acid tyrosine by tyrosinase. A distinct feature of the *Drosophila* melanoma is the precocious deposition of melanin within the tumor cell.

The foregoing statements represent the present thinking concerning the histogenesis of the *tu-e* melanoma. Less definite information is available concerning the lethal effects of this tumor. It does appear that this strain is more difficult to maintain than the non-tumorous, ebony-scarlet strain from which it was derived.

Several additional problems can be raised, the answers to which may shed light on the problem of mammalian tumor formation in general and on melanomas in particular. These are

1. the role of the gene in tumor cell induction
2. the factors involved in tumor localization
3. the relationship between tumor development and the hormones controlling growth and differentiation
4. the relationship between the tumor cells and the destruction of the tissues it infiltrates
5. the role of melanization in tumor development
6. the factors which govern the specific pattern of melanin deposition in the tumor mass.

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